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POST HERPES NMDAR ENCEPHALITIS IN A 8 MONTH OLD GIRL

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ABSTRACT:

Introduction: Patients with Herpes Simplex virus Encephalitis are seen to have a relapse of symptoms namely seizures and choreoathetoid movements along with impairment of consciousness[1]. Though infective relapse is a possibility requiring extended antiviral therapy[2], immune mediated mechanism is most probable.[3] Although there is a similarity of symptoms between relapsing HSVE and N-methyl-D-aspartate receptor (NMDAR) antibody encephalitis, the most likely culprit is the latter.

Case Report: An appropriate for age 8 month old girl presented with fever and seizures. Cerebrospinal fluid was suggestive of viral encephalitis and Herpes PCR was positive. MRI Brain showed diffuse involvement. Acyclovir was started and she was administered two doses of IVIG. After almost 2 weeks of therapy she developed choreoathetoid movements. Repeat MRI showed progression of disease and CSF after three weeks of Acyclovir had Herpes PCR negative but was positive for NMDAR antibodies. A well-recognized condition treatable with early recruitment of immunomodulatory therapy

Key Words: autoimmune encephalitis, NMDAR, HSV,

INTRODUCTION:

Encephalitides are a well-known entity in Pediatric population with a wide variety of causative organisms having variable pathogenesis. Herpes simplex encephalitis (HSE) is a well-recognized condition with an increased mortality in the developed world.[1,2] Though the overall prognosis has markedly improved ever since Acyclovir, an antiviral drug, has been launched; still a remarkable 35% of affected patients end up with prolonged morbidity, severe neurological sequelae and even in mortality. Patients with Herpes Simplex Virus (HSV) Encephalitis are seen to have a relapse of symptoms namely seizures and choreoathetoid movements along with impairment of consciousness[3]. Though infective relapse is a possibility requiring extended antiviral therapy, more than three fourth of the patients have no infective evidence; making immune mediated mechanism most probable.[4,5] Many distinct neurological syndromes are recognized over the years in which antibodies directed towards the central nervous system have been identified, with a significant number of conditions featuring movement disorders.[6,7]

N-Methyl-D-Aspartate receptor (NMDAR) antibody encephalitis, having a myriad of symptoms ranging from seizures to psychiatric symptoms, bizarre movements to autonomic instability, has been recognized as an autoimmune encephalitis which can occur post HSV encephalitis.[8] This condition has a marked similarity to the choreoathetoid movements in relapsing Herpes simplex virus encephalitis (HSVE).[9]

CASE REPORT

An 8 months old child presented in the emergency with history of episodes of unresponsiveness for 10-15 seconds which resolved spontaneously. A day later she developed high grade fever and a generalized seizure. She was admitted in the nearby health facility and was treated along the lines of encephalitis/cerebral malaria. Her cerebrospinal fluid (CSF) done was unremarkable though she was started on Acyclovir 10 mg/kg/dose in 3 divided doses. She was started on antiepileptics as well but her seizures were not controlled for which she was brought to our hospital. On examination she was

afebrile with a GCS of 8/15, having partial seizures over her left arm intermittently. Her repeat CSF, showed a TLC of 10 with 95% lymphocytes and 5% neutrophils; Proteins 69 and glucose 62. PCR was positive for HSV 1 and oligoclonobands were negative. Her MRI Brain, Fig 1 showed abnormal signal intensities involving bilateral frontal, left parieto-occipital, right occipital lobes, antero-medial portion of both thalami identified and most of the corpus callosum. These abnormal signals, were hyper intense on T2 and FLAIR sequences and demonstrated diffusion restriction. A working diagnosis of acute necrotizing encephalomyelitis (Herpes virus) was made. Intravenous acyclovir was increased to 20mg/kg/dose in 3 divided doses. She was started on Phenytoin and Levetriacetam for seizure control. She was given Intravenous Immunoglobulins (IVIG) 1 gm/kg/day, 2 doses. Her condition started improving, started tolerating feed initially by orogastric tube and then by cup and spoon, responded to visual and auditory stimuli as well. After almost two weeks of therapy, she suddenly developed choreoathetoid movements, stopped focusing and the clinical course started downhill. Repeat MRI, Fig 2 showed progression of disease with no new development. CSF was done after completion of three weeks of acyclovir which came positive for NMDAR encephalitis and Herpes PCR was negative.

DISCUSSION

NMDAR encephalitis, is a recently recognized autoimmune encephalitis, not even a decade old; more and more evidence is being collected in favor of a strong relationship between viral infections and antibody production directed against the central nervous system. Though this relationship is much more intricate thereby requiring prospective studies in children with suspected encephalitides. Deficient innate immunity is postulated to be a susceptibility factor for Herpes Viral Encephalitis but has not been linked to autoimmune encephalitis.

With more cases being reported in literature with post herpetic NMDAR encephalitis especially in the pediatric population, there is increasing evidence that the viral etiology serves to induces the NMDAR antibodies which causes the illness after the resolution of the acute phase.

Panzer et al studied a group of 44 but the youngest patient was 12 years old. Course of the disease with suggestive CSF findings and response to treatment depending upon the extent of the disease matches our patient. Large scale studies are still required for a better insight regarding the management of the disease. Therefore if a patient relapses without any evidence of Herpes reactivation, an autoimmune etiology especially NMDAR antibody should be considered as a strong possibility and the treatment protocols consisting of immunomodulation should be followed to avoid excessive damage to the already affected brain.

Fig 1. MRI brain, coronal section showed abnormal signal intensities involving bilateral frontal, left parietal-occipital, right occipital lobes and antero-medial portion of both thalami

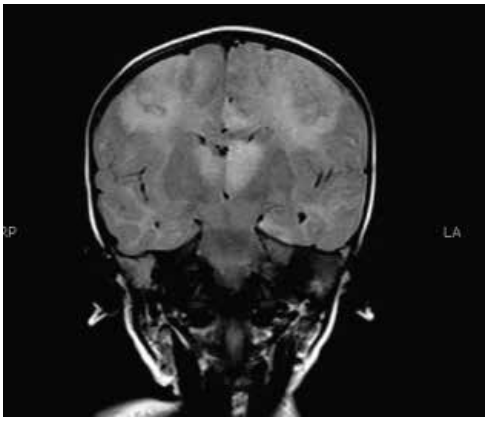
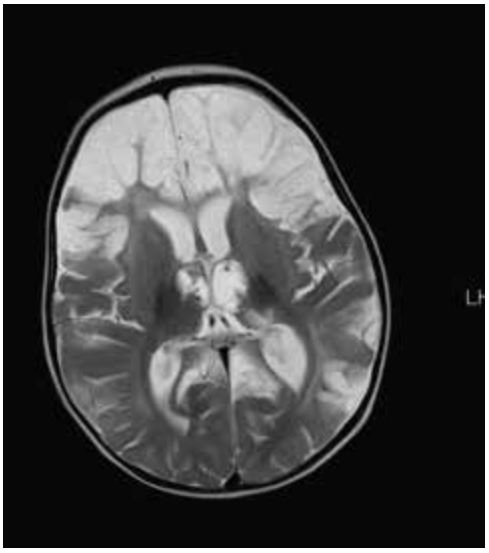


Fig 2. Repeat MRI brain, axial section T2 images showing hyper intense signals corresponding to the areas of involvement but more profound



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Author's contribution:
Farida Jan; data collection, data analysis, manuscript writing, manuscript review
Shahnaz Hamid Ibrahim; data collection, data analysis, manuscript writing, manuscript review